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(54) Oral Hygiene Composition

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ABSTRACT

ORAL HYGIENE COMPOSITION

An oral hygiene composition comprises effective amounts of a cationic anti-bacterial agent and a polymer which bears pendant polyalkylene side-chains and preferably carboxylic acid groups. Such compositions reduce both the bio-fouling of teeth and the staining thereof which may arise from the interaction of the cationic bacterial agent with dietary components.

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ORAL HYGIENE COMPOSITION

This invention relates to oral hygiene compositions and to methods of using such compositions to prevent or inhibit growth of bacteria on tooth surfaces.

The prevention of the adherent deposition of dental plaque on mammalian (particularly human) teeth is a highly desired result. Dental plaque results when cariogenic and other types of bacteria aggregate in colonies on the surface of teeth and form a deposit which adheres tenaciously to the surface. It is believed that the deposition of plaque on the surface of a tooth is one of the first steps in the development of dental caries and periodontal disease.

Many attempts have been made to prevent the deposition of plaque on tooth surfaces and to effect removal of plaque from such surfaces. For example, brushing, dental flossing and the use of oral irrigators and interdental stimulators have been tried. Such treatments are not, however, entirely successful and must often be supplemented with periodic treatment by dental professionals.

In our recently published European Patent Specification No 0,182,523A, we teach that certain pharmaceutical compositions (as therein defined) are highly effective for preventing or significantly reducing (a) the colonisation of tooth surfaces or simulated tooth surfaces by cariogenic and other micro-organisms commonly found in an oral environment, and (b) the adherent deposition on tooth surfaces of dental plaque resulting from such microorganisms.

The preparation of polymers for use in the aforesaid certain pharmaceutical compositions is described in EP 0,182,523A.

Chlorhexidine is a cationic antiseptic which has been widely used by the medical profession as a topical antibacterial agent for more than 20 years; the preparation thereof is described in UK 705,838. It has been reported (Löe et al, Journal of Periodontal Research, 1970, Vol 5, pp79-83) that chlorhexidine can be used as an antiseptic in the oral environment and that in certain circumstances there is a tendency apparently for chlorhexidine to stain teeth. Such staining appears to be a property which is common to cationic antiseptics. It has been shown (Addy et al, Journal of Periodontal Research, volume 9, pp 134-140) that such staining is the result of an interaction between the cationic antiseptic and dietary components, particularly those rich in tannins, e.g. coffee, tea or red wine.

We have now found that where certain surfaces, e.g. tooth, or hydroxyapatite, are treated with a combination of both (a) a
polymer, as hereinafter defined, which bears certain pendant polyalkylene oxide chains, and (b) a cationic antibacterial agent, the resulting treated tooth surfaces surprisingly exhibit both enhanced antiadhesive and antibacterial properties to certain oral micro-organisms, i.e. the combination may effect control of so-called "bio-fouling" of tooth surfaces.
Indeed, in the presence of the said polymer, equivalent antibacterial effects can be observed where the tooth surface is treated with a lower concentration of a solution of the antibacterial agent. Furthermore, we have now found, surprisingly, (i) that the aforesaid tendency for staining with chlorhexidine is at least reduced, there is often no increase in staining even where more chlorhexidine is adsorbed on the tooth surface in the presence of the aforesaid polymer; (ii) the antibacterial properties of certain cationic

antibacterial agents, e.g. chlorhexidine and alexidine, are increased on simulated tooth surfaces if the surface is treated sequentially with or with a a combination of, an acidic polymer, e.g. Polymer 93W (as hereinafter defined)and the aforesaid agent ; and (iii) where composite restorations, e.g. Occlusion (RTM), Opalux, Silux and Valux P50, etc, tend to be stained by cationic antiseptics such staining is at least alleviated in the presence of the aforesaid polymer. It will be appreciated that reduction at least of such staining of anterior teeth is particularly desirable.

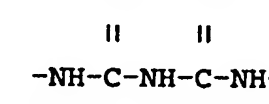
According to the present invention there is provided an oral hygiene composition comprising

(i) an effective amount of a cationic antibacterial agent; and

(ii) an effective amount of at least one polymer ,as hereinafter defined, which has one or more pendant polyalkylene oxide groups.

As examples of cationic antibacterial agents which may be used in the present invention may be mentioned inter alia benzalkonium chloride, bispyridinamines, e.g. octenidine, or preferably a poly-biguanide, e.g. alexidine, or more preferably a bis-biguanide, eg chlorhexidine.

By "polybiguanide" we mean a compound which has a plurality of in-chain biguanide residues of the general formula I

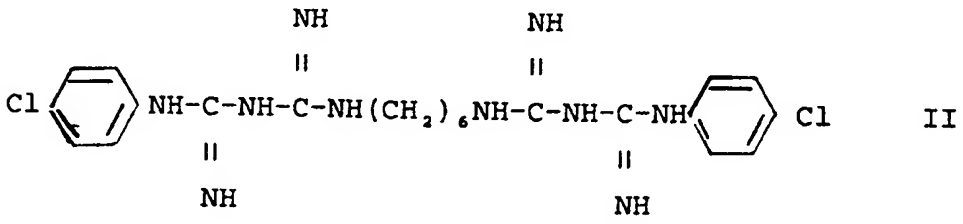


I

or tautomers thereof. Often there are two, three or four such in-chain residues in the antibacterial agent used in the present invention. However, we do not exclude the possibility that there may be sufficient to provide at least a major portion of the repeat units of a higher

molecular weight polymer, e.g of molecular weight up to about 10,000.

It will be appreciated that where a polybiguanide is used in the present invention it may be present as a free base; preferably, however, it is present as a salt thereof, e.g. acetate or hydrochloride, or more preferably, particularly where the polybiguanide is a bis-biguanide which has the structure shown in general Formula II, as the di-gluconate, i.e. the di-gluconate of 1,6-di(4-chlorophenyl-diguanido)hexane, which is known in the art as chlorhexidine.



II

We do not exclude the possibility that where a polybiguanide, e.g. chlorhexidine, in the form of a free base is used in the present invention it may be in admixture (e.g. as a salt) on the tooth surface as a salt with an acidic polymer as hereinafter defined.

As possible explanations, without wishing to be bound thereby, of the increased antibacterial effect of the oral hygiene composition of the present invention, we suggest:

(i) an increase in the quantity of chlorhexidine adsorbed on the tooth surface; and/or

(ii) alteration in the strength of adsorption of chlorhexidine at the tooth surface such that it is more available to exert its antibacterial effect at the surface; and/or

(iii) alteration in the orientation at the tooth surface of adsorbed chlorhexidine such that the

antibacterial groups thereof are more accessible to bacteria approaching thereto; and/or

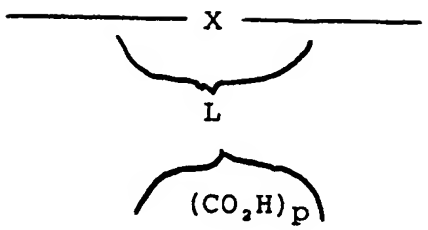
(iv) ion-pairing between the cationic antibacterial agent and the acid anions, where present, of the polymer.

In the composition according to the present invention, multiple hydrogen-bonds between the polymer, and the biguanide cations may contribute to the aforesaid increase in quantity or alteration in strength of adsorption or orientation.

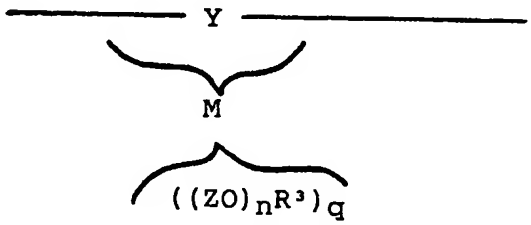
Polymers of which the oral hygiene composition according to the present invention are comprised are preferrably acidic, by which we mean that there is at least one carboxylic acid group appended to the polymer backbone. However, we do not exclude the possibility that the polymer may be amphoteric, basic or neutral, although this not preferred.

The one or more pendant polyalkylene oxide groups appended to the polymers of which oral hygiene compositions according to the present invention are comprised are preferably ethylene oxide groups. However, we do not exclude the possibility that at least a portion thereof may be alternative poly(lower)-alkylene oxide groups, e.g. polypropylene.

As examples of polymers of which the oral hygiene composition according to the present invention are comprised may be mentioned inter alia polymers which comprise one or more repeating units of general structure A



and one or more repeating units of general structure B



wherein X, which in the repeating units of structure A may be the same or different, and Y, which in the repeating units of structure B may be the same or different, are hydrocarbyl, or substituted hydrocarbyl residues, providing a backbone for the polymer;

Z is $-CHR^1-CHR^2-$ or $-(CH_2)_m-$; wherein, where Z is $-CHR^1-CHR^2-$,

R^1, which in the same repeating unit of structure B (when n or q is 2 or more) or in different repeating units of structure B may be the same or different, is hydrogen or a hydrocarbyl group; and

R^2, which in the same repeating unit of structure B (when n or q is 2 or more) or in different repeating units of structure B may be the same or different, is, hydrogen or a hydrocarbyl group; except that R^1 and R^2 in a single unit $-CHR^1-CHR^2-O-$ cannot both be hydrocarbyl;

R^3, which in the same repeating unit of structure B (when q is 2 or more) or in different repeating units of structure B may be the same or different, is hydrogen or a hydrocarbyl group or an acyl group derived from an alkanoic acid having up to five carbon atoms;

m, where present, is a number of from 2 to 10;

n is a number of from 1 to 60;

p is a number of from 1 to 4; and

q is a number of from 1 to 4;

each (CO_2H) group is joined via an intermediary or intermediaries L to the hydrocarbyl residue X, and in cases where p is 2 to 4 may be joined by L to the same or different carbon atoms of X;

L may be the same or different in the repeating units of structure A and is selected from one or more direct links and one or more groups of atoms each group providing a chain of one or more atoms for linking a (CO_2H) group with X, except that more than two (CO_2H) groups cannot be directly linked to the same carbon atom in X;

each $((ZO)_nR^3)_q$ group is joined via an intermediary or intermediaries M to the hydrocarbyl residue Y, and in cases where q is 2 to 4 may be joined by M to the same or different carbon atoms of Y;

M may be the same or different in the repeat units of structure B and is selected from one or more direct links and one or more groups of atoms each group providing a chain of one or more atoms for linking a $(ZO)_n$ group with Y, except that more than two $(ZO)_n$ groups cannot be directly linked to the same carbon atom in Y;

the ratio of the number of $-CO_2H$ groups to the number of (ZO) groups, particularly where Z is $-CH_2CH_2-$, is within the range of 1:20 to 20:1

Preferably both R^1 and R^2, where they are present, are hydrogen.

Where R^1 or R^2 is a hydrocarbyl group, it is preferably a lower alkyl group, more preferably methyl.

R^3 is preferably a lower alkyl group, more preferably methyl.

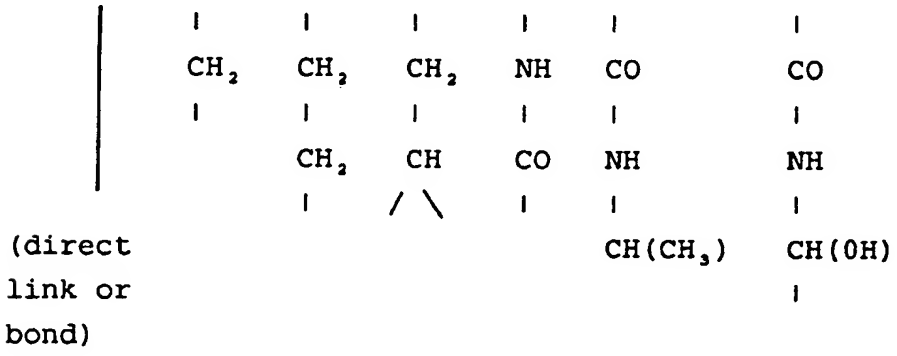
Where Z is $-(CH_2)_m-$, m is preferably 4; this affords a ready preparation of $-(ZO)_n-$ from tetrahydrofuran.

It is to be understood that the definition of the polymer contained in the composition (as given above) is also intended to embrace a polymer in which at least some of the carboxyl groups in the repeat units of general structure A have been converted to the corresponding salt anions CO_2- (these being considered as $-CO_2H$ group as far as the ratio of carboxyl to -ZO- groups is concerned), the corresponding cations for example being those of ammonium ($NH+_4$), or alkaline earth metals or preferably alkali metals (e.g. Na+, K+). We do not exclude the possibility that the cation may be derived from the cationic antibacterial agent per se; indeed where the cationic antibacterial agent is present as a salt of the acid polymer such that there is substantially no free chlorhexidine in the mouth there is a tendency for staining to be further reduced.

In general structure A, each carboxyl group is joined to the hydrocarbyl residue X by means of an intermediary or intermediaries (i.e. by a linking entity or entities), this or these being denoted by L, which is selected from one or more direct links (i.e. one or more direct bonds) and one or more groups of atoms each group providing a chain of one or more atoms for linking a carboxyl group(s) with X. In cases where p is 2 to 4, each carboxyl group may be joined by L to the same or, in cases where L represents more than one intermediary, to

the same or different carbon atoms in X, although more than 2 carboxyl groups cannot of course be directly linked to the same carbon atom of X (and also assuming that in such cases X has at least 2 carbon atoms, whereas it should be appreciated that it is within the scope of the invention for X to have only 1 carbon atom). It will be noted that in principle L can represent up to 4 separate intermediaries in structure A (in cases where p is 4). L may be the same or different in the repeat units of structure A.

In cases where L represents one or more groups of atoms each group providing a linking chain of atoms, the chain will normally comprise one or more carbon atoms (which could, for example, include carbon atoms in an aryl ring) and/or hetero atoms (particularly N and/or O). Examples of possible linkages provided by L are:

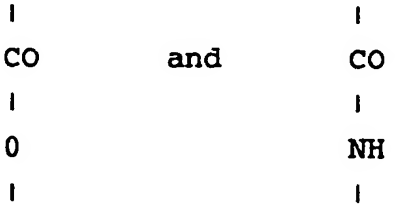


where (apart from the direct link) the top link is to X and the bottom link(s) is to carboxyl. It is preferred in the present invention, however, that L is one or more direct links, such that each carboxyl group is joined directly to a carbon atom in the polymer backbone.

In the structure A, p is preferably 1 or 2, more preferably 1 (so that L can then represent one, or at most, two intermediaries).

In structure B, each $(ZO)_n R^3$ group is joined to the hydrocarbyl residue Y by means of an intermediary or intermediaries (i.e. by a linking entity or entities), this or these being denoted by M, which is selected from one or more direct links (i.e. one or more direct bonds) and one or more groups of atoms each group providing a chain of one or more atoms for linking a $(ZO)_n R^3$ group(s) with Y. In cases where q is 2 to 4, each $(ZO)_n R^3$ group may be joined by M to the same or, in cases where M represents more than one intermediary, to the same or different carbon atoms in Y, although more than two $(ZO)_n R^3$ groups cannot of course be directly linked to the same carbon atom of Y (and also assuming that in such cases Y has at least 2 carbon atoms, whereas it should be appreciated that it is within the scope of the invention for Y to have only 1 carbon atom). M may be the same or different in the repeat units of structure B.

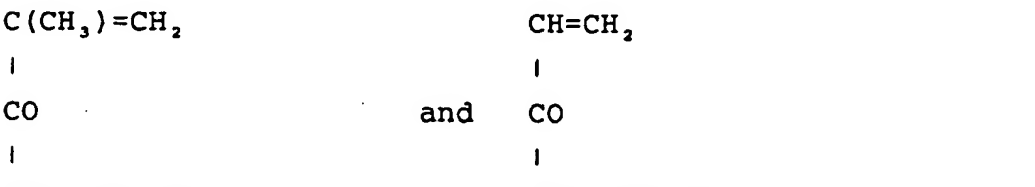
While M may represent one or more direct links, it is preferred in the present invention that M is one or more groups of atoms each group providing a linking chain of atoms; such a chain will normally comprise one or more carbon atoms (which could, for example, include carbon atoms in an aryl ring, e.g. benzyl ether) and/or hetero atoms (particularly N and/or 0). Particularly preferred examples of chains provided by M are:



where the top link is to Y and the bottom link is to $(ZO)_n R^3$.

In structure B, q is preferably 1 or 2, more preferably 1(so that M can then represent one, or at most two intermediaries).

Preferably the structure A represents the repeat unit derivable by the addition polymerisation (usually free-radical initiated) of a polymerisable olefinically unsaturated carboxylic acid. Examples of such acids are maleic (or fumaric) acid, itaconic acid, the acids of formulae



N-methacryloyl alanine— and N-acryloyl-hydroxy-glycine

or preferably acrylic or methacrylic acid

Preferably the structure B represents the repeat unit derived from the polymerisation (usually free-radical initiated) of an addition polymerisable olefinically unsaturated ester or amide formed from the reaction of an unsaturated carboxylic acid (or an esterifiable or amidifiable derivative thereof such as an acid chloride or anhydride) and a hydroxy compound of formula $HO\ (ZO)_n\ R^3$ (to form the ester) or an amine of formula $H_2N\ (ZO)_n\ R^3$ (to form the amide).

Preferably the acid from which structure B is derivable is acrylic or methacrylic acid, particularly the latter, giving rise, where an ester or amide derivative of methacrylic acid is used, to the following structures respectively for B:

$$-C(CH_3)---CH_2--$$
$$|$$
$$CO$$
$$|$$
$$O\ (ZO)_n\ R^3,$$

and

$$-C(CH_3)---CH_2--$$
$$|$$
$$CO$$
$$|$$
$$NH\ (ZO)_n\ R^3$$

Preferably acidic polymers of which oral hygiene compositions according to the present invention are comprised have a ratio of acidic residues to pendant polyalkylene oxide residues of about 6:1 (where each side chain is polyethylenegylcol of molecular weight about 350, i.e. so-called PEG 350).

Polymers for use in the present invention are more fully described in our aforesaid European Patent Specification No 0,182,523A.

In oral hygiene compositions of the present invention, the at least one polymer present therein is typically at least at a concentration of about 0.05 to 30 weight % of the composition, the preferred concentration range being from about 0.1 to 5 weight % and more preferably 0.2 to 2 weight %.

The concentration of the at least one antibacterial agent in oral hygiene compositions according to the present invention is about 0.001 to 10 weight % of the composition, the preferred concentration range being from about 0.001 to 1.0 weight % and more preferably 0.01 to 0.1 weight %.

Preferably, the mass of the polymer is higher than the mass of the anti-bacterial agent in oral hygiene composition according to the present invention. However, we do not exclude the possibility that there may be more anti-bacterial agent than polymer present.

The oral hygiene composition of the present invention typically comprises only one polymer as hereinbefore defined, although we do not exclude the possibility that two or more such polymers may be present in the composition.

The skilled man by simple experiment will be able to formulate compositions according to the present invention in which the ratio of antibacterial agent to polymer is such that undesired reaction is avoided.

The oral hygiene composition of the present invention typically comprise a pharmaceutically acceptable vehicle which is compatible with the antibacterial efficacy of the cationic antibacterial agent, e.g. chlorhexidine. To maintain the efficacy of chlorhexidine it may be necessary to adjust the concentration thereof in a particular vehicle, a suitable concentration may be determined by the skilled man by experiment.

Suitable conventional pharmaceutically acceptable vehicles that can be employed in the oral hygiene compositions of the present invention include water, ethanol (wherein water, or a water/ethanol mixture will often be a major component of the vehicle); such humectants as propylene glycol, isopropanol, glycerol and sorbitol; such gelling agents as cellulose derivatives, for example, hydroxypropyl and hydroxyethyl cellulose, polyoxypropylene/polyoxyethylene block copolymers, (so-called "Poloxamers"), for example Synperonic* PE 39/70 and PEF 87; certain gel stabilisers such as polyvinylpyrrolidone; sweeteners such as sodium saccharin; preservatives such as cetylpyridinium chloride, and certain lower alkyl parahydroxy-benzoates; surfactants such as polyoxyethylene isohexadecyl ether (Arlasolve*200) and certain colours and flavours, on the

* Trade Mark

approved EEC or FD&C lists. It will be appreciated that the aforesaid vehicle is chosen such that it does not unduly inhibit the effectiveness of the oral hygiene composition according to the present invention; in particular, an anionic material, eg an anionic cellulose derivative or an anionic Synperonic, is not preferred.

The oral hygiene compositions of the present invention may be in the form of any conventional pharmaceutically acceptable oral hygiene formulation that contains (and is compatible with) an effective amount of a polymer and antibacterial agent as hereinbefore defined. As examples of such formulations may be mentioned inter alia mouthwashes, rinses, irrigating solutions, abrasive and non-abrasive gel dentifrices, denture cleansers, coated dental floss, coated or impregnated toothbrush bristle (natural or synthetic), inter-dental stimulator coatings, chewing gums, lozenges, breath fresheners, foams and sprays.

The present invention is now illustrated by the following Examples. The prefix "CT" to an Example number denotes a Comparative Test.

In most of the following Examples the oral bacterium Streptococus mutans NCTC 10449 was used as the standard bacteria. It was grown in Brain Heart Infusion (BHI) (ex Oxoid) in a Bioflo Model C30 Fermenter. A 750 ml pot was used containing 350 ml of bacterial suspension. The bacteria were grown at 37°C with a dilution rate of $0.1h^{-1}$, an air flow of 0.24 litre/minute and an agitation speed of 300 rpm. A sample (approximately 20 ml) of bacterial suspension was taken out of the fermenter for each experiment. The bacteria were centrifuged for 10 minutes at 4000 rpm, they were resuspended in modified Ringer's salts solution (0.54 grams/litre NaCl; 0.02 grams/litre KCl; 0.03 grams/litre

$CaCl_2$; and 0.75 grams/litre sodium mercaptoacetate), recentrifuged,
resuspended and diluted (10 x) in modified Ringer's salts solutions. The approximate bacterial concentration in the diluted salts solutions was 10^8 ml^{-1}.

Streptococcus mitior

NCTC 7864 was grown in 100ml Brain Heat Infusion broth in batch culture for 24 hours. The culture was then centrifuged for 30 minutes at 3500rpm and washed twice by resuspending the pellet in saline and centrifuging. The bacterial suspension was then adjusted to approximately 10^7-10^8 cells per ml.

Whole saliva was used in further examples.

Absorption surfaces

Hydroxyapatite discs were made by compressing hydroxyapatite powder (calcium phosphate tribasic ($Ca_{10}(OH)_2(PO_4)_6$ (ex Aldrich)) and sintering at 1100°C. The discs were re-used after heating in a furnace at 900°C for 2 hours between experiments.

Application of polymers

Hydroxyapatite discs were treated for 2 minutes at room temperature with a solution (1% w/v) of a polymer, e.g. Polymer 93W, in a 1:1 (by volume) mixture of industrial methylated spirits/water. The discs were then washed by dipping and shaking 5 times in a container of flowing water at about 15°C.

Application of Anti-Bacterial Agent

Aqueous solutions of chlorhexidine and IMS solutions of alexidine were separately adsorbed for certain periods of time onto the surfaces of hydroxyapatite discs which had been treated with polymer where appropriate (untreated discs were used in comparative tests). The discs were then washed by dipping and shaking 5 times into a container of flowing water.

Polymers

The polymer herein referred to as "Polymer 93W" is an acidic polymer as described and prepared in Example 5 of our aforesaid EP.182523. (Other "acidic" polymers hereinafter described were prepared by a similar process). Polymer 93W comprises methacrylic acid and PEG350MAt residues in molar ratio 6: 1.

By "PEG350MAt" we mean a polyethylene oxide of molecular weight about 350 which has been capped with methoxy and methacryloyl groups, i.e.

$CH_2=C(CH_3)COO(CH_2CH_2O)_nCH_3$ where n is about 8.

PEG 150Mat, PEG1000 Mat and PEG 2000 Mat indicate similar polyethylene oxides of molecular weights 150, 1000 and 2000 respectively.

Polymer M11 was prepared under the conditions described in Example 15 of EP 182,523 except that a hydroxy ended PEG was used instead of an amino ended PEG.

Loeffler's Methylene Blue

95% Ethyl alcohol (30 ml), methylene blue (0.3 g) and water (100 ml).

Examples 1-2

These Examples demonstrate that Polymer 93W retains its anti-adhesive properties in the presence of absorbed chlorhexidine.

Hydroxyapatite discs were treated with a 1% w/w solution of Polymer 93W and then with certain antibacterial agents for set periods of time. The discs so treated were immersed in a bacterial suspension (30 mls) in a petri-dish for 2 hours. The discs were removed from the bacterial suspension and were washed by dipping and shaking 5 times in a container of flowing water. Bacteria adhering to the discs were stained using Loeffler's Methylene Blue. The reduction in bacterial adhesion was determined by microscopic examination.

The results are shown in Table 1.

TABLE 1

Example No	Antibacterial Agent	Polymer	% Anti-adhesion
CT1	0	1%93 W	99
1	C	1%93 W	99
2	A	1%93 W	99

CT1: 1% 93W was used alone
C: 1% chlorhexidine
A : 1% alexidine

From Table 1 it can be seen that chlorhexidine and alexidine do not reduce the anti- adhesive properties of Polymer 93W deposited on hydroxyapatite discs.

"%Anti-adhesion" ("% AA") is defined by the equation:

$$\%AA = \frac{\left(\begin{array}{l}\text{Area of neat surface}\\ \text{covered with bact.}\end{array}\right) - \left(\begin{array}{l}\text{Area of polymer-coated}\\ \text{surface covered with bact.}\end{array}\right)}{\left(\begin{array}{l}\text{Area of neat surface}\\ \text{covered with bacteria}\end{array}\right)}$$

It will be appreciated that (a) where the polymer does not decrease the area of the surface which is coated with bacteria then:

$$\% AA = \frac{X-X}{X} \times 100 = 0$$

and (b) where the polymer prevents adhesion of bacteria to the surface then:

$$\% AA = \frac{X-O}{X} \times 100 = 100$$

Similar results were obtained when a specimen of material conventionally used in the preparation of a dental prosthetic device, as hereinafter described, was treated with polymer 93W and chlorhexidine was then exposed to Streptococcus mitior NCTC 7864.

EXAMPLES 3-5

These Examples demonstrate that on hydroxyapatite the antibacterial effect of chlorhexidine at certain concentrations is increased where it is used in the presence of Polymer 93W.

Solutions of chlorhexidine were absorbed onto sterile hydroxyapatite discs which had been treated with Polymer 93W. Cells of S. mutans were taken from a fermenter and diluted 100 fold in BHI agar at 40°C. The innoculated agar was overlayed onto HAP discs.

Agar coated discs were incubated at 37°C overnight. Bacterial growth throughout the agar was assessed on a scale of 0 (no growth) to 10 (control).

Since the surface of each hydroxyapatite disc was brought into contact with the same number of bacteria in each case, anti-adhesion did not contribute to the observed result, i.e. antibacterial effect alone was being measured. The results in Table 2 reveal that the combination of Polymer 93W and chlorhexidine gave an enhanced antibacterial effect compared to chlorhexidine per se at the same applied concentration of chlorhexidine.

In Comparative Tests CT's 2, 3, 4 and 5, the discs were not treated with Polymer 93W. Comparative Test 2 is a blank; in Comparative Test 2A, the disc was treated with Polymer 93W only.

TABLE 2

Example No	Applied Chlorhexidine concentration	Treatment with Polymer 93W	Bacterial growth
CT2	0	NO	10
CT2A	0	YES	10
CT3	1	NO	8
CT4	0.1	NO	10
CT5	0.01	NO	10
3	1	YES	0
4	0.1	YES	2
5	0.01	YES	4

EXAMPLES 6-9

These Examples demonstrate the combination of anti-adhesive and antibacterial results which can be obtained from the use of a combination of a polymer and chlorhexidine and that such a combination provides an improvement over the discrete components per se.

Sterile hydroxyapatite discs were treated with a 1% w/v solution of Polymer 93W and then with solutions of certain concentrations of chlorhexidine. The discs were incubated in freshly collected whole saliva for 1 hour at 37°C and washed by dipping and shaking 5 times into a container of flowing water. Excess water was removed from the surface of each disc by touching the edge thereof with filter paper.

BHI agar containing 0.04% w/v Bromo Cresol Green (to render bacterial growth on the white hydroxy-apatite discs visible) was pipetted at 40°C onto the discs such that a thin film of agar formed on the surface.

The discs were incubated at 37°C overnight.

The results are shown in Table 3.

In Comparative Tests 6-10 the treatment with Polymer 93W was omitted. In Comparative Test 11, Polymer 93W was used, in the absence of chlorohexidine.

TABLE 3

Example No	Concentration of chlorhexidine (%)	Presence of Polymer 93W	Bacterial growth
CT6	1	NO	No Growth
6	1	YES	No growth
CT7	0.1	NO	Control level 4.
7	0.1	YES	No Growth
CT8	0.01	NO	Control level 5.
8	0.01	YES	A few colonies; greater than 99% reduction compared with control level 5
CT9	0.001	NO	Control level 6.
9	0.001	YES	99% reduction compared with control level 6
CT10	0	NO	Thick Growth: control level 7
CT11	0	YES	90% Reduction compared with CT7 control level 7

From Table 3 it can be seen that for certain concentrations of chlorhexidine, e.g. 0.01 and 0.001%, the presence of Polymer 93W increases the bactericidal and/or bacteriostatic effect thereof. CT11 demonstrates the reduction in bacterial growth which arises from the anti-adhesion properties of the polymer per se.

EXAMPLES 10-20

These Examples reveal that treatment of hydroxyapatite discs with certain polymers

(a) increases the amount of chlorhexidine absorbed thereon and

(b) improves the retention of the absorbed chlorhexidine through subsequent washing treatments.

Preparation of Polymers B3 and B18

Methacryloyl chloride (0.58 moles) was added over 2 hours to a mixture of toluene (600 ml), Jeff "360" or "2070" (0.5 moles) and 2,6-lutidine (0.56 moles) cooled in an ice-bath. A copious white precipitate formed. The reaction mixture was allowed to stand for 3 hours, and the white precipitate was filtered off and washed with toluene. The filtrate was evaporated under reduced pressure and the residue was kept under vacuum to remove volatiles. Products (yield 80-90%) were characterised by infra-red and proton magnetic resonance spectroscopy.

The amino-ended products from both reactions (with terminal butoxy or methoxy groups from "360" and "2070" respectively) were separately converted into the N-methacrylaloyl derivatives thereof and copolymerised with methacrylic acid under the conditions described in Example 11 of EP 0.182,523A.

Hydroxyapatite discs were pre-equilibrated in double distilled water for 1 hour. The discs were removed from the water, blotted dry and kept at room temperature for about 30 minutes. A UV reflectance scan

thereof was carried out. The Optical Density at 266 nm was typically about 0.9. Any disc which had an O.D. which was significantly different from this number was rejected.

The acceptable discs were immersed in 1% w/w (1:1/IMS: water) solution of polymer for 5 minutes. The discs were removed from the polymer solution; were washed by dipping and shaking 5 times in a container of flowing water; were blotted dry; left for 30 minutes and then scanned.

Each of the polymer-coated discs was immersed in aqueous (15 ml) chlorhexidine solution (0.02% w/v) for 1 hour. They were washed as described above, allowed to stand for 30 minutes and then scanned. They were then placed in a flow-through (250 ml/min) washing tank (1200 ml) for 1 hour; blotted dry; allowed to stand for 30 minutes and scanned.

TABLE 4

Example Number	Polymer	Applied Chlorhexidine Concentration %	Difference in Optical Density at 266 nm over blank H A disc	% Chlorohexidine retained after washing for	
				1 hour	17 hours
CT12	73	0.02	0.01	nd	nd
CT13	B12	0.02	0.02	nd	nd
10	62	0.02	0.12	80	49
11	86	0.02	0.15	93	58
12	93W	0.02	0.20	79	47
13	66	0.02	0.12	82	39
14	B9	0.02	0.22	82	50
15	58	0.02	0.14	86	68
16	B3	0.02	0.22	82	45
17	B10	0.02	0.19	77	54
18	B18	0.02	0.30	85	57
19	B17	0.02	0.25	77	66
20	M11	0.02	0.23	b	b
CT14	PMMA	0.02	0.02	nd	nd
CT15	None	0.02	0.01	nd	nd
CT16	None	0.2	0.06	nd	nd
CT17	None	2	0.18	23	nd

PMMA: Polymethacrylic acid.
n.d.: Not detected, i.e. below detection limit.
b: Not determined.
The meanings ascribed to the polymers listed in Table 4 are shown in Table 5.

TABLE 5

Polymer	A Backbone Nature (Source)	B Side Chain Mol Wt	Molar Ratios A:B	Molar Ratios $CHR^1CHR^2O:CO_2H$ groups
73	Basic (DMAEM)	PEG 350	3:1	
B12	Amphoteric (MAA:DMAEM)	PEG 350	1.9:1.1:1	
62	Acidic (MAA)	PEG 150	3:1	1:1
86	Acidic (MAA)	PEG 350	3.5:1	2.3:1
93W	Acidic (MAA)	PEG 350	6:1	1.3:1
66	Acidic (MAA)	PEG 1000	3:1	7.7:1
B9	Acidic (MAA)	PEG 1000	25:1	0.9:1
58	Acidic (MAA)	PEG 2000	10:1	4.5:1
B3	Acidic (MAA)	Jeff 360	6:1	1.1:1
B10	Acidic (MAA)	Allyl-PEG 350	6:1	1.3:1
B18	Acidic (MAA)	Jeff2070	34:1	1.2:1
B17	Acidic (MAA)	PPG 1000	17:1	1:1
M11	Acidic (MAA)	PEG 350	5:1	0.9:1

DMAEM:N N-dimethyl-2-aminoethyl methacrylate.

MAA: Methacrylic acid.

MA: Maleic acid;

PEG: Polyethylene glycol.

PPG: Polypropylene glycol;

Jeff 360 : $n\text{-}C_4H_9(OCH_2CH_2)_4OCH_2CH(CH_3)OCH_2CH(CH_3)NH_2$;

Jeff 2070: $CH_3OCH_2CH_2O(CH_2CHO)_nCH_2CH(CH_3)NH_2$

$$\begin{array}{c} | \\ R \end{array}$$

wherein n is such that "2070" has an MW of about 2000 and R = H or CH_3 in a ratio of about 7:3;
Allyl-PEG 350: Ethoxylated allyl alcohol;
Except for B10, the methacrylate or methacrylamido derivatives of the indicated side chains were present as general structure B;
B10: contains terminal hydroxy groups.

The aforesaid UV scanning was effected using a Unican SP1750 Ultraviolet Spectrophotometer.

The "difference in Optical Density" results shown in Table 4 were determined therefrom.

From Tables 4 and 5, it can be seen that the acidic polymers significantly increased the amount of chlorhexidine absorbed. Many of the hydroxyapatite surfaces coated with an acidic polymer absorbed more chlorhexidine from a 0.02% w/v solution than did the neat hydroxyapatite surface from a 2% w/v solution of chlorhexidine, i.e. a greater than a 100-fold improvement was observed. The basic (Polymer 73) and amphoteric (Polymer B12) polymers gave no improvement in the amount of chlorhexidine adsorbed. Similarly, polymethacrylic acid yielded no increase in chlorhexidine adsorbed, indicating that it was the PEG (or PPG) chains, and not the carboxyl groups, that were responsible for the observed effect.

The results of the washing experiments showed that after 1 hour about 23% of the initially adsorbed chlorhexidine was still adsorbed on bare hydroxyapatite discs, whereas the amount for polymer treated discs was approximately 80%. After an overnight wash, the amount of adsorbed chlorhexidine, if any, remaining on the neat HAP discs was below the detection limit; and approximately 50-60% of the amount of chlorhexidine

originally adsorbed on polymer-treated discs remained adsorbed. Thus, polymer-treated discs adsorbed more chlorhexidine than bare discs, and it was also less easily washed off the surface thereof.

EXAMPLES 21-29

These Examples, in combination with Examples 10-20 and 6-9, reveal an increase in anti-bacterial properties (at a certain chlorhexidine concentration) without the expected increase in staining.

General Procedure

Hydroxyapatite discs were pre-equilibrated in double- distilled water for 1 hour. The pre-equilibrated discs were immersed in 1% w/v aqueous or IMS:water (1:1) solution of polymer for 5 minutes. They were removed from the polymer solution and washed by dipping and shaking 5 times in a container of flowing water. The washed discs were then immersed in 15 ml of an aqueous chlorhexidine solution (of a concentration shown in Table 6) for 5 minutes. The discs were removed from the chlorhexidine solution and immersed in 15 ml of a tea solution for 1 hour at room temperature. The discs were taken out of the tea solution and washed as described above. The steps of immersion in chlorhexidine and tea solution and washing were repeated 3 times, using fresh chlorhexidine and tea solutions each time. After these three cycles the discs were immersed in tea solution overnight; they were then washed as described above, allowed to dry for 1 hour at room temperature and the amount of stain produced thereon was assessed.

The tea solution was prepared by adding 500 ml of boiling water to 2 tea bags. The tea bags were removed after 5 minutes, and the tea allowed to cool to room temperature. The tea was filtered using standard filter paper, and stored at 4°C prior to use.

The stained discs prepared in the General Procedure were scanned using UV/visible reflectance spectrophotometry as described in Examples 10-20 and compared with tea blanks (i.e. no chlorhexidine adsorbed). Figure 1 shows typical UV- traces which were obtained. In Figure 1, a = bare hydroxyapatite disc; b = tea blank; and c,d,e, = tea/chlorhexidine treatments at 0.002%, 0.02% and 0.2% concentrations of chlorhexidine respectively.

The polymers listed in Table 6 (the chemical composition of which are given in Table 5) were evaluated for their effect on the stain formation of chlorhexidine in the presence of tea. The polymers were separately adsorbed from 1% w/v IMS/water (1:1) solutions. 0.2%, 0.2% and 0.002% w/v aqueous solutions of chlorhexidine were used. The discs were scanned using UV/visible reflectance spectrophotometry and the OD's at 266, 410 and 510 nm were measured. The OD's of tea blanks were also measured at these wavelengths, and these values were subtracted from discs treated with chlorhexidine or polymer/ chlorhexidine combinations. Table 6 gives the results at 510 nm. They are expressed as ratios relative to the stain produced by a tea blank = 1.0. Similar results were obtained at 266 nm and 410 nm. In CT 18, the polymer was omitted, i.e. chlorhexidine per se was used.

TABLE 6

Comparative Stain Development compared with "Natural" build-up from exposure to tea solutions.

Example No	Polymer	O.D. Ratio (compared with natural tea stain) at 510 nm at applied Chlorhexidine Concentrations of		
		0.2%	0.02%	0.002%
CT18	-	4.57	2.76	1.67
21	73	4.48	3.01	1.0
22	62	4.98	2.65	1.0
23	86	4.48	3.26	1.0
24	93W	4.98	2.79	1.0
25	B9	4.75	3.09	<1.0
26	B3	4.39	3.34	1.0
27	B10	4.76	3.34	<1.0
28	B18	4.20	3.12	<1.0
29	B17	5.03	2.95	<1.0

From Table 6 it can be seen that at the two higher chlorhexidine concentrations (i.e. 0.2 and 0.02%) the presence or nature of the polymer had no substantial effect on the amount of stain produced on treatment of HAP discs. At the lowest concentration (i.e. 0.002%) of applied chlorhexidine, the majority of Examples show a significant reduction in stain equal to or less than the minimal levels associated with exposure of HAP discs to the tea solutions. However, it will be appreciated from the results in Examples 10-20 and 6-9, that, for about the same stain as the control, the polymers had more

chlorhexidine absorbed thereon and exhibited an increased antibacterial effect.

EXAMPLES 30-31

These Examples illustrate the increase in the quantity of chlorhexidine adsorbed onto a hydroxyapatite disc treated with a mixture of chlorhexidine and Polymer 93W compared to treatment of the HAP disc with a chlorhexidine solution per se.

An IMS solution (2% w/v) of Polymer 93W was mixed with an appropriate (0.04% w/v) solution of chlorhexidine in water, at a solution ratio of 1:1 by volume. Hydroxyapatite discs were allowed to stand in the mixture for 1 hour and were then washed five times with water. The amount of chlorhexidine absorbed on the discs was determined by UV reflectance spectrophotometry as described in Examples 10-20 (the Optical Density was measured at 266 nanometers).

In Comparative Tests 20 and 21, the discs were treated for 1 hour with 0.2 and 0.02 % solutions respectively of chlorohexidine in a 1:1 by volume mixture of industrial methylated spirit and water.

The results are shown in Table 7. From Table 7 it can be seen that treatment of a HAP with the Polymer 93W/chlorhexidine mixture results in more chlorhexidine being absorbed than from chlorhexidine solution per se.

TABLE 7

Example No	State of addition of composition	Concentration of chlorhexidine % w/v	Increase in Optical Density at 266 nm
30	Mixture	0.2	0.44
31	Mixture	0.02	0.12
CT19	Neat chlorhexidine solution	0.2	0.0
CT20	Neat chlorhexidine solution	0.02	0.0

EXAMPLES 32-33

These Examples illustrate the increased "kill" of a Polymer 93W/chlorhexidine mixture compared with that observed with neat chlorhexidine solution.

The discs prepared in Examples 30-31 were washed overnight in water and subjected to an S.mutans agar overlay experiment. They were placed in a petri-dish and covered with BHI agar (25 mls). S mutans (100 µl), grown in a fermenter (as described above) and diluted x 100 in Ringers salt solution, was pipetted onto the agar and evenly spread. The bacteria were grown overnight at 37°C; "lawns" of bacteria and "clear zones" free of bacteria were noted and measured. The results are shown in Table 8. The clear zones, i.e. zones where growth did not occur, are shown as a percentage of the area of the disc.

TABLE 8

Example No	Disc Prepared in Example No	Concentration of chlorhexidine % w/v	% Area of disc where growth did not occur
32	30	0.2	225
33	31	0.02	64
CT21	CT19	0.2	3
CT22	CT20	0.02	0

It will be appreciated that where "% Area of disc where growth did not occur" is more than 100, this indicates that inhibition spread into the agar layer beyond the perimeter of the disc.

From Table 8, it can be seen that the mixture has an increased antibacterial activity compared with chlorhexidine per se.

EXAMPLES 34-65

These Examples show that the combination of an anti-adhesive compound, Polymer 93W, and chlorhexidine reduce the amount of staining, compared with chlorhexidine per se, generated on a variety of surfaces found in the oral environment. The surfaces comprised tooth, composite restorative materials, e.g. Occlusin and Opalux, and a methacrylate-based resin conventionally used in the preparation of dental

prosthetic devices (hereinafter referred to for convenience as "PR").

SPECIMENS

Residual flesh was removed with a scalpel from freshly extracted teeth, the teeth were then tumbled for 20 minutes in 50% sodium hypochlorite solutions and washed superficially with distilled water.
These and teeth containing restorative material were sonicated in alcohol for 10 minutes and then dried.

Samples of DR (25 mm x 10 mm x 3 mm) and discs of the aforementioned composite restoratives were washed in alcohol and dried.

SOLUTIONS

a 1% and 0.5% solutions of Polymer 93W (1gm) in a mixture of industrial methylated spirit (50 ml) and water (50 ml).

b Solutions (0.2%, 0.02%, and 0.002%) of chlorhexidine in water.

c Appropriate mixtures of Polymer 93W and chlorhexidine were obtained by mixing equal volumes of solutions from a and b to afford the concentrations shown in the folowing Tables.

d Human saliva was obtained by taking specimens (20 mls) from each of 6 volunteers, centrifuging for 20 minutes at 2,5000 rpm and pooling them.

e Tea solution was prepared by boiling a sample (8g) of a commercial brand of tea in distilled water (80 ml) for 2 minutes, cooling the product to room temperature and filtering off the residual tea leaves.

Evaluation

Each surface was treated for 10 minutes with a sample of the saliva. Excess saliva was washed off.

In Examples 34-49, the surface was subjected to a first treatment for 10 minutes, superficially washed with distilled water, subjected to the second treatment for 10 minutes, rinsed and then immersed in the tea

solution for 1 hour; the procedure was repeated, the sample was left in the tea solution overnight and the whole procedure repeated every day for 5 days.

In examples 50-65 the above 5 day procedure was repeated except that the first treatment was for 5 minutes and the second treatment was omitted, the samples were treated with appropriate mixtures of Polymer 93W and chlorhexidine.

The staining of the surfaces was compared visually with the same surface treated only with water and scored on the following scale.

Scale

0 : No stain (ie Water-control taken as 0, although there was slight discolouration);
1 : Slight stain;
2 : Moderate stain;
3 : Heavy stain; and
4 : Very heavy stain.

In Tables 9, 10 and 17

OC = Occlusin
OP = Opalux
T = Tooth
PR = Prosthetic resin
A = 0.5% Polymer 93W
AA = 1% Polymer 93W
B = Water
X = 0.1% Chlorohexidine
XX = 0.2 "
Y = 0.01 "
YY = 0.02 "
Z = 0.001 "
ZZ = 0.002 "
W = 0.0001 "

TABLE 9

Example No	Surface	Treatments		Score
		First or Single (10 mins)	Second (10 mins)	
CT23	OC	B		0
CT24	OP	B		0
CT25	T	B		0
CT26	PR	B		0
CT27	OC	X		3
CT28	OP	X		3
CT29	T	X		3
CT30	PR	X		3
CT31	OC	AA		0
CT32	OP	AA		0
CT33	T	AA		0
CT34	PR	AA		0
34	OC	AA	XX	3
35	''	''	YY	1
36	''	''	ZZ	0
CT35	''	B	XX	3
CT36	''	''	YY	2
CT37	''	''	ZZ	1
37	OP	AA	XX	4
38	''	''	YY	2
39	''	''	ZZ	0
CT38	''	B	XX	3
CT39	''	''	YY	2

TABLE 9 - Cont

Example No	Surface	Treatments		Score
		First or Single (10 mins)	Second (10 mins)	
CT40	OP	B	ZZ	1
40	T	AA	XX	4
41	''	''	YY	2
42	''	''	ZZ	0
CT41	''	B	XX	3
CT42	''	''	YY	2
CT43	''	''	ZZ	1
43	PR	AA	XX	4
44	''	''	YY	2
45	''	''	ZZ	0
CT44	''	B	XX	3
CT45	''	''	YY	2
CT46	''	''	ZZ	1
46	OC	XX	AA	0
47	OP	''	''	0
48	T	''	''	0
49	PR	''	''	0

TABLE 10

Example No	Surface	Treatment (mixture for 5 mins)	Score
CT47	OC	B	0
CT48	OC	X	4
CT49	OC	Y	3
CT50	OC	Z	1
CT51	OC	W	1
CT52	OC	A	0
50	OC	A+Y	2
51	OC	A+Y	0
52	OC	A+Z	0
53	OC	A+W	0
CT53	OP	B	0
CT54	OP	X	4
CT55	OP	Y	3
CT56	OP	Z	1
CT57	OP	W	1
CT58	OP	A	0
54	OP	A+X	4
55	OP	A+Y	3
56	OP	A+Z	1
57	OP	A+W	1

TABLE 11

Example No	Surface	Treatment (mixture for 5 mins)	Score
CT59	T	B	0
CT60	T	X	4
CT61	T	Y	3
CT62	T	Z	1
CT63	T	W	1
CT64	T	A	0
58	T	A+X	2
59	T	A+Y	0
60	T	A+Z	0
61	T	A+W	0
CT65	PR	B	0
CT66	PR	X	4
CT67	PR	Y	2
CT68	PR	Z	1
CT69	PR	W	1
CT70	PR	A	0
62	PR	X	2
63	PR	Y	0
64	PR	Z	0
65	PR	A+W	0

From Table 9, it can be seen that at low concentration (eg 0.002%) of chlorhexidine staining of dental restorative, teeth or prosthetic resin is reduced if the surface thereof is first treated with a certain polymer. It can be seen further (Examples 46-49) that where the surfaces are treated with a

chlorhexidine solution and then with Polymer 93W the staining is reduced to control levels.

Table 10 reveals the results obtained on treating Occlusin and Opalux surfaces with mixtures of chlorhexidine and Polymer 93W. There is a significant reduction in the staining of Occlusin, to control levels at chlorhexidine concentrations of 0.01% and less; a similar trend is apparent with Opalux.

Table 11 reveals the results obtained on treating tooth surfaces and a prosthetic resin with a mixture of chlorhexidine and Polymer 93W. The trend in the reduction in staining is similar to that observed with Occlusin and Opalux.

Where a tooth with an Occlusin implant was subjected to the above evaluation, the tooth and implant were slightly stained to the same extent such that the outline of the implant was further decreased.

CLAIMS

1. An oral hygiene composition which comprises

(i) an effective amount of at least one cationic anti-bacterial agent which is a benzalkonium chloride, a bispyridinamine, or a poly-biguanide; and

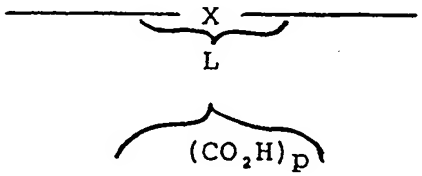
(ii) an effective amount of at least one polymer which bears pendant polyalkylene oxide side-chains.

2. An oral hygiene composition as claimed in Claim 1 wherein the catonic anti-bacterial agent is a polybiguanide or a salt thereof.

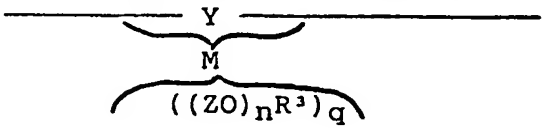
3. An oral hygiene composition as claimed in Claim 2 wherein the polybiguanide is a bis-biguanide.

4. An oral hygience composition as claimed in Claim 3 wherein the bis-biguanide is chlorhexidine.

5. An oral hygiene composition as claimed in Claim 1 wherein the least one polymer comprises one or more repeating units of general Structure A.



and one or more repeating units of general structure B



wherein X, which in the repeating units of structure A may be the same or different, and Y, which in the repeating units of structure B may be the same or different, are hydrocarbyl, or substituted hydrocarbyl residues, providing a backbone for the polymer;

Z is $-CHR^1-CHR^2-$ or $-(CH_2)_m-$; wherein, where Z is $-CHR^1-CHR^2-$

R^1, which in the same repeating unit of structure B (when n or q is 2 or more) or in different repeating units of structure B may be the same or different, is hydrogen or a hydrocarbyl group; and

R^2, which in the same repeating unit of structure B (when n or q is 2 or more) or in different repeating units of structure B may be the same or different, is, hydrogen or a hydrocarbyl group; except that R^1 and R^2 in a single unit $-CHR^1-CHR^2-O-$ cannot both be hydrocarbyl;

R^3 which in the same repeating unit of structure B (when q is 2 or more) or in different repeating units of structure B may be the same or different, is hydrogen or a hydrocarbyl group or an acyl group derived from an alkanoic acid having up to five carbon atoms;

m, where present, is a number of from 2 to 10;

n is a number of from 1 to 60;

p is a number of from 1 to 4; and

q is a number of from 1 to 4;

each CO_2H) group is joined via an intermediary or intermediaries L to the hydrocarbyl residue X, and in cases where p is 2 to 4 may be joined by L to the same or different carbon atoms of X;

L may be the same or different in the repeating units of structure A and is selected from one or more direct links and one or more groups of atoms each group providing a chain of one or more atoms for linking a (CO_2H) group with X, except that more than two

(CO_2H) groups cannot be directly linked to the same carbon atom in X;

each $(ZO)_nR^3)_q$ group is joined via an intermediary or intermediaries M to the hydrocarbyl residue Y, and in cases where q is 2 to 4 may be joined by M to the same or different carbon atoms of Y;

M may be the same or different in the repeat units of structure B and is selected from one or more direct links and one or more groups of atoms each group providing a chain of one or more atoms for linking a $(ZO)_n$ group with Y, except that more than two $(ZO)_n$ groups cannot be directly linked to the same carbon atom in Y;

the ratio of the number of $-CO_2H$ groups to the number of (ZO) groups, particularly where Z is $-CH_2CH_2-$, is within the range of 1:20 to 20:1

6. An oral hygiene composition as claimed in claim 5 wherein,where Z is $-CHR^1-CHR^2-$, both R^1 and R^2 are hydrogen.

7. An oral hygiene composition as claimed in claim 5 where R^3 is methyl.

8. An oral hygiene composition as claimed in claim 5 wherein, in structure A, L is a direct link,

$-CH_2-$, $-CH_2-CH_2-$, $-CH_2-CH$ =, -NH-CO-,
- $CONHCH(CH_3)$- or -CONHCH(OH)-

9. An oral hygiene composition as claimed in Claim 5 wherein, in Structure A, p is 1 or 2.

10. An oral hygiene composition as claimed in Claim 5 wherein, in structure B, M is -COO-or CONH-

11. An oral hygiene composition as claimed in Claim 5 wherein, in structure B, q is 1 or 2.

12. An oral hygiene composition as claimed in Claim 5 wherein A or B represents the repeat unit derivable by

the addition-polymerisation of a polymerisable olefinically unsaturated carboxylic acid or an ester or amide derivative thereof respectively.

13. An oral hygiene composition as claimed in Claim 12 wherein the polymerisable olefinically unsaturated carboxylic acid is acrylic acid or methacrylic acid.

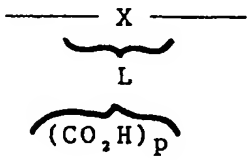
14. An oral hygiene composition as claimed in Claim 1 comprising a pharmaceutically acceptable vehicle which is water, ethanol, a humectant, gelling agent, gel stabiliser, sweetener, preservative, surfactant or an approved colour or flavour.

15. An oral hygiene composition as claimed in Claim 1 the form of mouthwash, rinse, irrigating solution, gel dentifrice, denture cleaner, coated dental floss, coated or impregnated tooth-brush bristle, inter-dental stimulator or coating, chewing gum, lozenge, breath freshener, foam or spray.

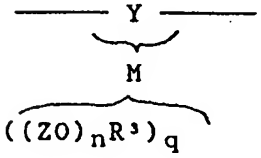
16. An oral hygiene composition which comprises

(i) an effective amount of from about 0.001-10 weight% of the composition of at least one cationic anti-bacterial agent selected from the group consisting of benzalkonium chloride, a bispyridinamine and a polybiguanide; and

(ii) an effective amount of from about 0.05-30 weight% of the composition of at least one polymer which comprises one or more repeating units of General Structure A



and one or more repeating units of general Structure B



wherein
X is $-CH_2-C(CH_3)-$
L is a direct link; and
p is 1; and wherein
Y is $-CH_2-C(CH_3)-$
M is -COO-
R^3 is methyl;
n is about 8;
q is 1; and
Z is $-CHR^1-CHR^2$, wherein R^1 and R^2 are hydrogen; and wherein the ratio of repeating units of general structure A to repeating units of general structure B is about 6:1.

17. The use of an oral hygiene composition according to any one of claims 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16 to prevent or inhibit growth of bacteria on tooth surfaces.

B

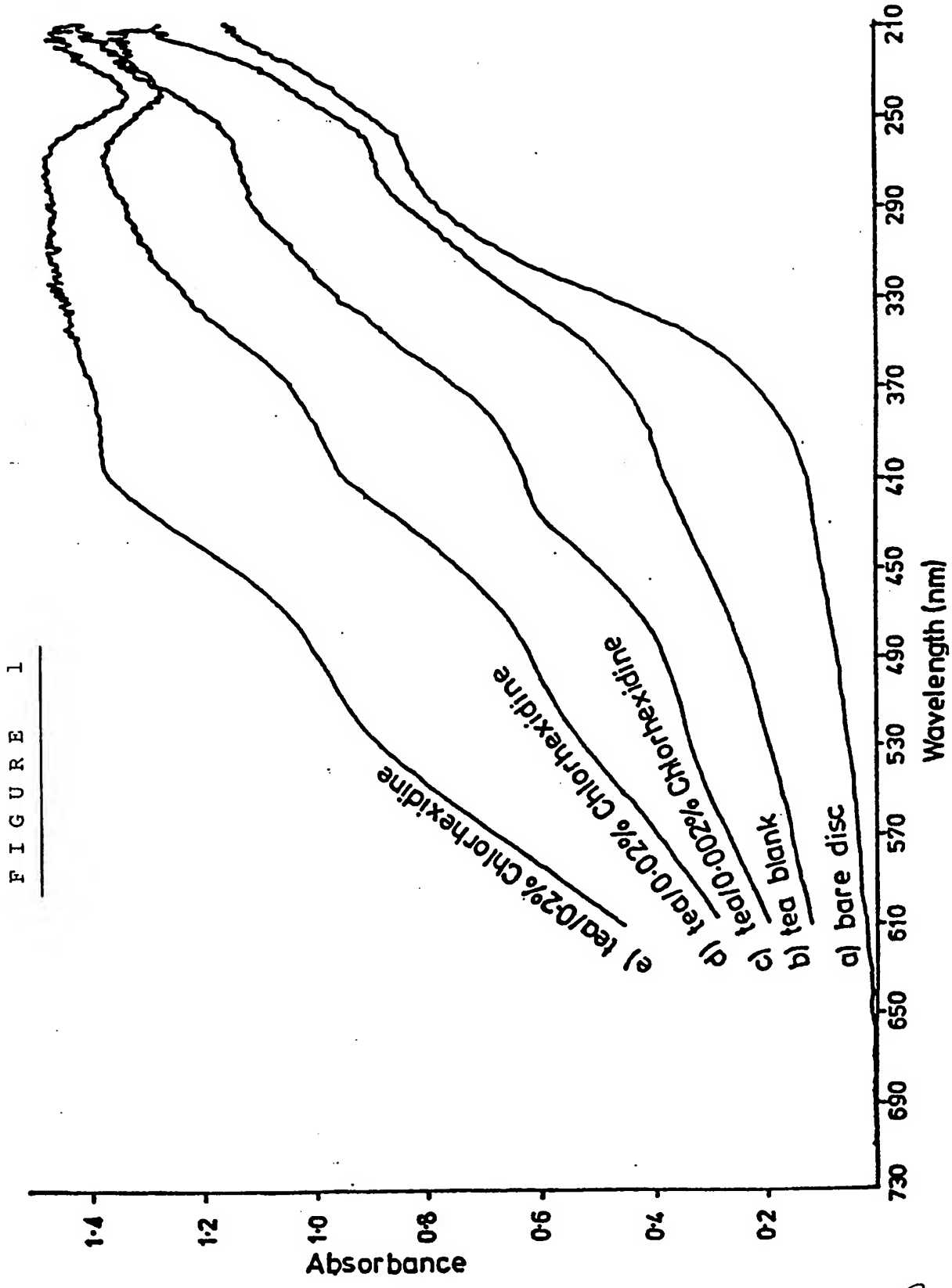


FIGURE 1

C. Brian Barker

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